

Attorney Docket Number O 99473 US

III. Remarks**A. Rejection Under 35 USC §112, 2nd ¶**

Claims 10 and 11 stand rejected as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regards as the invention because the Examiner contends the phrase "each pair" is indefinite. The Examiner queries whether "pair" refers to two of the same progestagens administered or one of anti-progestagen dose with other active agents. Applicants respectfully request reconsideration of the rejection in light of this response.

Applicants have amended Claims 10 and 11 to add "said" after "each of." Accordingly, the Claims are not indefinite and Applicants respectfully request reconsideration of the rejection in light of the amendment. Such amendment is not limiting and no estoppel should result.

B. Rejections Under 35 USC §103

Claims 2, 4, 10-14 and 16-18 stand rejected as being unpatentable over WO 93/21927 to Hodgen (hereinafter referred to as the '927 patent) in view of publication XP-002124156 to Schoonen et al (hereinafter referred to as the Schoonen publication) and US Pat No. 5,854,235 to Hamersma (hereinafter referred to as the '235 patent). The Examiner contends that the '927 patent teaches a method of minimizing menstrual bleeding irregularities in individuals using progestin-only pharmaceutical preparation, such as contraceptive, such as administering anti-progesterone such as Org 31710. The Examiner directs attention to the abstract, p. 5, ll. 20-30 and p.7, ll. 20-32. The Examiner further contends that the '927 patent teaches that the antiprogesterone can be administered monthly, or at other intermittent levels, p.9, ll. 32-36. The Examiner further asserts that the '927 patent further teaches that a suitable regimen is an antiprogesterone administered every 30 days, every 60

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days or every 90 days and in the case of contraceptives, the antiprogesterin can be administered on the 28th day of each cycle, p. 10, ll. 5-20.

The Examiner then contends that the Schoonen article teaches that anti-progestinic activity of Org 33245 is compared to that of Org 31710, in vitro and in vivo. The Examiner contends that it is shown that Org 33245 is more active than Org 31710, abstract, p. 164, table, rt hand column, ll. 18-24, p. 167, rt. Column, ll. 1-7.

The Examiner then contends that the '235 patent teaches that Org 33245 is useful in contraception and it exhibits the normal activities known for antiprogesteragen, such as the treatment of menstrual disorders and hormone dependent tumors.

The Examiner surmises that difference between the '927 patent and Applicants' Claims are that Applicants utilize Org33245 as the anti-progesteragen and the dosage schedule as set forth in Claim 4. The Examiner concludes that it would have been obvious to one of ordinary skill in the art to modify the '927 patent to employ Org 33245 in the place of Org 31710 to achieve the benefit of increased activity of antiprogesterin therapy for the contraception and decreased menstrual disorders, such as bleeding. The Examiner contends that absent any evidence to the contrary, there would have been a reasonable expectation of successfully employing Org 33245 in the method of the '927 patent for hormone replacement therapy. Further, the Examiner concludes that the dosage schedule is obvious because it falls within the normal dosing of a contraceptive.

Applicants respectfully request reconsideration in light of this argument.

To begin, the '927 patent only describes the protracted administration of progestogen with administration of an antiprogesterational compound on the 28th or 30th day of the treatment cycle. The '927 patent does not teach or suggest, however, a method of the treatment of contraception or hormone

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replacement therapy using Org33245 wherein said compound is to be administered intermittently, the intermission between each pair of sequentially administered dosage units of anti-progestogen being more than one day. In fact, the '927 patent does not even mention Org 33245, let alone intermittent administration of Org 33245.

Moreover, the '235 patent only discloses a series of 17-spiromethylene steroids, including Org 33245, and indicates that the compounds are useful as contraceptives and useful in the treatment of menstrual disorders and for hormone dependent tumors. The '235 patent does not teach or disclose treatment regimes or dosage schedules. Accordingly, the '235 patent does not teach or disclose a method of the treatment of contraception or hormone replacement therapy using Org33245 wherein said compound is to be administered intermittently, the intermission between each pair of sequentially administered dosage units of anti-progestogen being more than one day.

Likewise, the Schoonen publication describes several anti-progestogens, one of which is Org 33245. While it is true that the Schoonen publication teaches that the activity of Org 33245 is higher than that of Org31710, the publication also teaches that the activity of Org 33628 is higher than that of Org 33245. However, this has no bearing.

The Examiner is contending that Org 33245, being more active than Org 31710, could be substituted for said compound in the '927 patent's method. Therefore, by the same line of reasoning, Org 33628 ought to be able to be substituted for Org 33245 of Org 31710. However, as indicated in the specification, Org 33628 is metabolized to rapidly, the half life is about 12 hours in humans. (See p. 3, ll. 11-14).

Further, the Schoonen publication only addresses in vitro and in vivo antiprogestogen activities of a selection of compounds including Org 33245 and Org 33628. The publication does not deal with the

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stability or duration of action of either compound. A person skilled in the art would have no teaching that Org 33245 would have a sufficient duration of action such that it would be suitable for the purposes of the present invention (or in fact that Org 3324 would be preferable over Org 33628).

However, Applicants' invention, for the first time, illustrated that Org 33245 is preferable over Org 33628 in an intermittent range. In fact, Org 33245 has a surprisingly better suitability than the other tested Orgs for being administered intermittently. Further, Org 33245 has a surprisingly strong binding to human orosomucoid, which is indicative of a relatively long half life. This statement is supported by the instant application's specification in the Table on page 9 where experimental values for binding affinity are given.

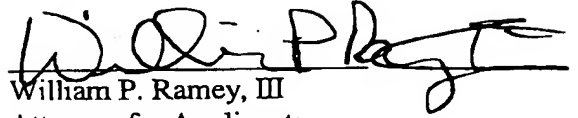
In conclusion, Applicants assert that neither the '927 patent, the '235 patent, and/or the Schoonen publication, either alone or in combination teach or suggest a method of the treatment of contraception or hormone replacement therapy using Org 33245 wherein said compound is to be administered intermittently, the intermission between each pair of sequentially administered dosage units of anti-progestogen being more than one day. Accordingly, Applicants assert that the instant invention is not obvious and respectfully request removal of the rejection.

IV. Conclusion

Applicants respectfully request reconsideration of the rejection in light of the amendments and argument. The Claims are believed in a condition for allowance and such action is requested. Applicants respectfully request the Examiner contact the undersigned attorney to facilitate allowance of the case. Please charge any required fees and credit any credits to deposit account 02-2334.

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Respectfully submitted,



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